REVIEW ARTICLE

Postoperative Care Following Pancreatic Surgery

Surveillance and Treatment

Volker Keim, Ernst Klar, Michael Poll, Michael H. Schoenberg

SUMMARY

Background: After pancreatic surgery, some patients have complications that require treatment.

Method: Review article based on a selective literature search and the German S3 guideline on pancreatic carcinoma.

Results: Detailed knowledge of the surgical procedure and its potential early and late complications is a prerequisite for the recognition and treatment of problems occurring after pancreatic surgery. These may be due either to the operation itself or to the progression of the underlying pancreatic disease. Both diabetes mellitus and exocrine insufficiency are common long-term sequelae. If persistent pain should arise, its cause must be identified and treated. To prevent malnutrition and vitamin deficiency after pancreatic resection, patients should be given a diet with an increased fat content and with supplemental enzymes.

Conclusion: Appropriate methods are available for the accurate diagnosis and, in most cases, successful treatment of complications arising after pancreatic surgery.

Key words: pancreatectomy, surgical treatment, postoperative phase, diagnosis, morbidity

Cite this as: Dtsch Arztebl Int 2009; 106(48): 789–94
DOI: 10.3238/arztebl.2009.0789

Department für Innere Medizin, Medizinische Klinik für Gastroenterologie und Rheumatologie, Universität Leipzig: Prof. Dr. med. Keim

Abteilung für Allgemeine, Thorax-,Gefäß-und Transplantationschirurgie, Universität Rostock: Prof. Dr. med. Klar

Lübbecke, Prof. Dr. med. Poll

Chirurg. Klinik, Rotkreuzklinikum München: Prof. Dr. med. Schoenberg

Since the initial description of a pancreatic resection by the Königsberg surgeon Walter Kausch in the year 1909 these operations have become part of the options for surgical treatment. This surgical technique was later termed the Whipple procedure. Over the years numerous other resection and drainage operations have been added. It is estimated that, in total, approx. 10 000 surgical pancreatic interventions are carried out per year in Germany. These operations are complex; the consequences arising from them are not easy to oversee for the attending physician. The aim of the following review is to present the diagnosis and therapy of medium and longterm sequelae of pancreatic surgery. A literature search of PubMed was carried out using the key words “pancreas, cancer, chronic pancreatitis, surgery”, and particular consideration was given to the German S3 guideline “Pancreatic Carcinoma.” (1).

Surgical treatment of pancreatic diseases

Indications

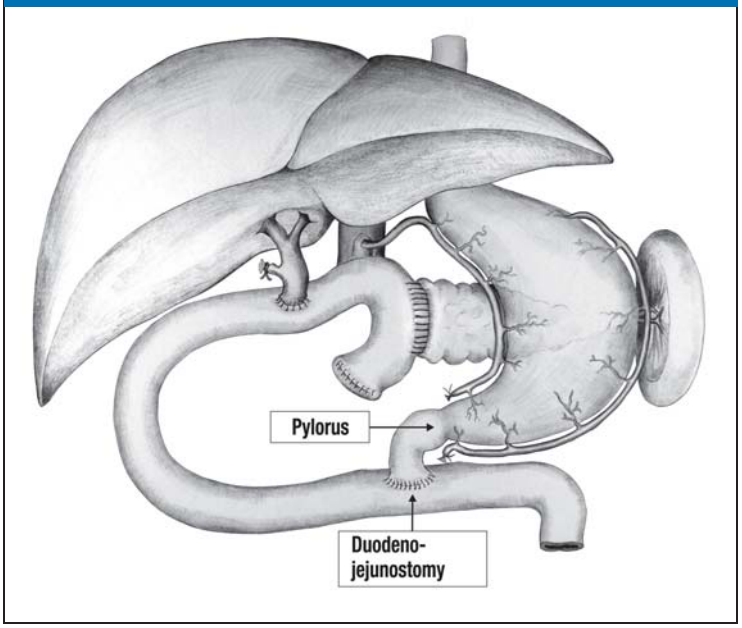
Operations on the pancreas are mainly carried out for pancreatic carcinoma, chronic pancreatitis and cystic tumors, less frequently for acute necrotizing inflammations of the pancreas.

For pancreatic carcinoma, complete surgical resection of the tumor (R0 resection) represents the only potentially curative therapy. This is, however, only successful in around 10% of patients, as very frequently, either the primary tumor is not locally resectable or alternatively, distant metastases are present. The 5-year survival rate following surgery and obligatory adjuvant chemotherapy is up to 23% (2). Two thirds of pancreatic carcinomas grow in the region of the pancreatic head.

The indications for surgery for chronic pancreatitis are upper abdominal pain which is difficult to control through medication, stenoses of the bile and pancreatic duct, the duodenum, and the portal vein. The goal of surgery, in addition to elimination of the abovementioned complications, is also long-standing absence of pain or alleviation of pain.

Cystic pancreatic tumors are operated on, where clinical symptoms are present and interventional therapy is unsuccessful, after clarification of the patient risk factors. In asymptomatic patients the decision for

FIGURE 1



Reconstruction after pylorus-preserving pancreatic head resection: The stomach remains preserved, the postpyloric duodenal segment (3 to 4 cm) is anastomized end-to-side onto the duodenal loop leading away from the pancreas and bile duct, 40 cm distal to the biliodigestive anastomosis (Chirug. Univ. Klinik Rostock)

or against surgery is based on the position, configuration, and contents of the cyst. Mucinous cysts should generally be surgically removed, as these can be precancerous, as should cysts with a high probability of malformation (mucinous cystadenomas).

Surgical procedures

In recent years there has been a clear move towards organ-preserving procedures, although for pancreatic carcinoma, the operation must be guaranteed to be sufficiently radical (3). For malignant tumors of the head of the pancreas, the Kausch-Whipple operation with pyloric sparing is usually the operation of choice, nowadays (*Figure 1*). By this means, the stomach remains intact in its entirety, the need for a surgical anastomosis is avoided, and the operating time is shortened (4). Its advantage from an oncological viewpoint is that the radicality of the procedure is not sacrificed (5). Delayed gastric emptying and food malabsorption can occur in just the first few days, but is as a rule reversible after 14 days (6).

One third of pancreatic carcinomas is found in the body and tail of the pancreas. In this case a leftsided resection is carried out with the aim of accomplishing a R0 resection.

Nowadays, in chronic pancreatitis, the inflammatory tumors of the pancreatic head are increasingly operated on in a way which preserves the duodenum. Two surgical procedures have thus established themselves (7, 8): duodenum-preserving pancreatic head resection described by Berger and local pancreatic head resection with longitudinal pancreaticojejunostomy known as Frey pancreatectomy (*Figures 2 and 3*). The long term results are admittedly similar to those of a Kausch-Whipple procedure, as both the frequency of diabetes, exocrine insufficiency, pain severity, and quality of life assessed by questionnaire were not different (9, 10). If an operation is required for chronic caudal pancreatitis, a left sided resection is carried out, where possible preserving the spleen. This is successful in almost half of the patients.

For cystic tumors in the pancreas corpus with no evidence of malignancy, segmental pancreatic resection is the surgical method of choice. The pancreatic duct and cut surface of the pancreatic head are oversewn. The tail of the pancreas is drained via a jejunal loop. This operation eliminates the pathology, clarifies dignity, and is organ-conserving (11).

Early postoperative treatment

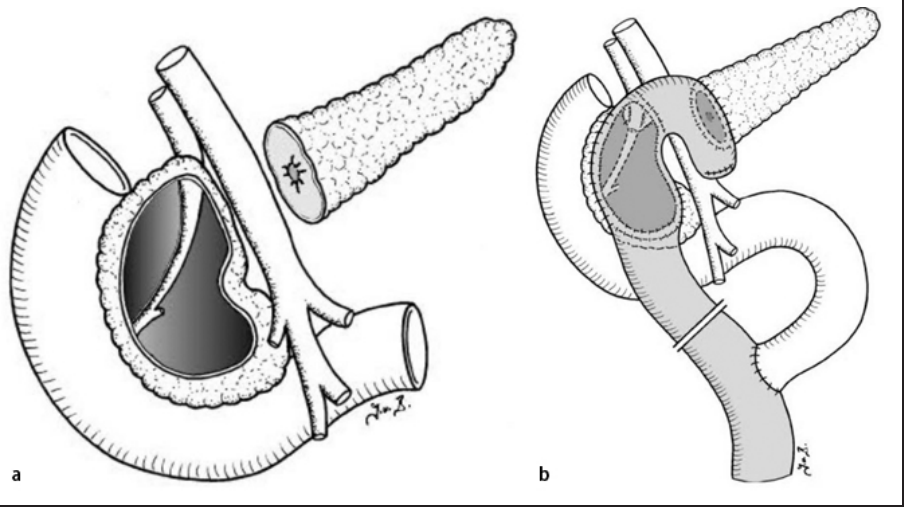
Hospital stays vary from 12 to 23 days, depending on the seriousness of the intervention. The 30-day mortality should be under 5%; in large centers mortality rates of under 3% are achieved (12). Fistulas present a considerable postoperative problem (5% to 12%) as do bile leaks (2% to 6%). In approximately 5% to 10% of cases repeat laparotomy is necessary. These are complex operations, with a postoperative morbidity of 30% (13). The 1-year mortality for patients with chronic pancreatitis is below 8% and with pancreatic carcinoma at around 25% (2).

Following discharge from hospital, a number of concerns can arise for colleagues responsible for continuing care. These concern both the asymptomatic patient, and the identification, differential diagnosis, and therapy of possible late complications.

Aftercare of asymptomatic patients

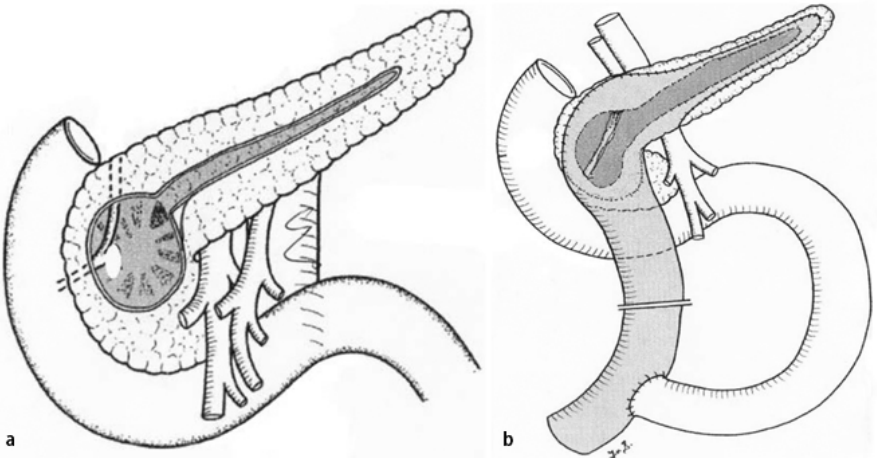
No aftercare is initiated for patients with no symptoms (patients who feel well, with no pain or weight loss).

FIGURE 2



Duodenum-preserving pancreatic head resection of the Berger type: after enucleation of the pancreatic head an anastomosis of the corpus and caudal pancreas and the remaining duodenal part of the pancreas is made with a loop of small intestine (from: Strobel O, Büchler MW, Werner J: Duodenumerhaltende Pankreaskopfresektion. Chirurg 2009; 80: 22–27; with kind permission of Springer Science and Business Media)

FIGURE 3



Local pancreatic head resection with longitudinal Frey pancreaticojejunostomy: in contrast with Berger pancreatic head resection, only a smaller portion of the pancreatic head is resected, the pancreatic duct is opened longitudinally and a loop of small intestine sutured over it (from: Strobel O, Büchler MW, Werner J: Duodenumerhaltende Pankreaskopfresektion. Chirurg 2009; 80: 22–27; with kind permission of Springer Science and Business Media)

This approach is supported by the S3 guideline "Pancreas Carcinoma" (1), which finds no evidence to support aftercare for this group. This contrasts starkly with the expectations of patients, who expect a high level of monitoring after major pancreatic surgery. It makes sense to undertake regular clinical examination of the patients (e.g. every 3 to 6 months) and repeat laboratory tests on parameters which were originally pathological. Similarly, examination is mandatory within the context of adjuvant chemotherapy. Should problems arise, symptom-orientated investigations are necessary. Regular blood glucose measurement is important (approximately every 3 to 6 months), as diabetes mellitus can develop both as a result of the pancreatic surgery and of progressing chronic pancreatitis. In patients with chronic pancreatitis, diabetes mellitus can be expected in 50% of cases after ten years' disease duration and in 80% after 20 years (20).

Late morbidity after pancreatic surgery

The late complications of pancreatic resection can be connected with the operation and the extent of the tissue resection itself and/or a result of progressive underlying disease and/or of continued alcohol and nicotine consumption. Longterm data are only available on a larger scale in patients with chronic pancreatitis as the survival time for pancreatic carcinoma is too short. The *Table* shows data from a long-term study with a 14 year follow-up (10). Despite the complexity of the surgery, the seriousness of the postoperative sequelae, and the rather unfavorable social integration of patients with chronic alcoholic pancreatitis over 40% of patients return to work.

Malnutrition and maldigestion

Pre- and perioperatively, many patients suffer significant weight loss (14). This can often be corrected only

TABLE

Late complications in patients with chronic pancreatitis after pancreatic surgery (10)

Complications	Frequency
Exocrine insufficiency	80%
Diarrhea	30%
Diabetes mellitus type IIIc	60%
Pain	30%
Stricture	18%
Inability to work	60%
Continued alcohol consumption	25%
Mortality	18%
Median follow-up time (years)	14

partially, in the postoperative period. The causes of the difficulty in regaining weight include recurrence of the pancreatic carcinoma, insufficient calorie intake, food intolerance, and exocrine insufficiency of the pancreas.

Low calorie intake

Patients are mostly advised to abstain from fat as far as is possible. This often leads to an impalatable diet which is deficient in calories. If fat is well tolerated and no steatorrhea arises, there is no call for this. Contrary to current, widespread recommendations, the fat content of the food should be increased to a target value of 30% (light normal diet), possibly with a corresponding increase in the dose of pancreatic enzymes (1). A somewhat higher fat content improves palatability and prevents fat-soluble vitamin deficiencies (A, D, E, K). Of course this measure must not be applied if attacks of pancreatitis are resultantly triggered or steatorrhea arises. In any case, food intake should be distributed over five to six meals. The use of medium-chain triglycerides (MCT lipids) is only necessary in very rare cases.

Intolerances arise in relation to various, e.g. bloating foods (cabbage, fiber). It is also possible for preexisting lactose intolerance to increase. A food diary can be useful for identification of these problems.

Exocrine insufficiency

Postoperative exocrine insufficiency is found in up to 80% of patients (10). The reason for this is the deficiency in glandular tissue, which is caused by the preexisting chronic pancreatitis and/or the pancreatic resection. However, the insufficiency only becomes manifest, if the (residual) pancreatic enzyme secretion has reduced to 10% to 15%. In addition, both after classic partial, as well as after pylorus-preserving duodenopancreatectomy, so-called pancreatico-cibal asynchrony occurs. This means that the pancreatic enzymes are secreted at the right time, but by virtue of the missing duodenum, only come into contact with the chymus in the mid jejunum—they are, so-to-speak, running behind the chymus. In addition, the so-called ileal break, the release of the hormones GLP-1 and PYY induced by the rapid passage of food into the ileum, leads to inhibition of pancreatic secretion and a reduction in appetite (15).

The symptoms of exocrine insufficiency are diarrhea, steatorrhea, abdominal pain, bloating, and weight loss. The investigations are difficult, as the available tests for pancreatic function such as the pancreolauryl test or stool elastase are only really conclusive if there is marked pancreatic insufficiency (16). Thus, with moderate insufficiency, their sensitivity is at only 65% (16). In addition, these tests are not validated for the postoperative period. Hence pancreatic enzymes are given exogenously, and can and must be dispensed generously. It should be remembered that, in patients who have undergone stomach resection or are taking proton pump inhibitors, absent or insufficient alkalization limits or delays the termination of acid protection, reducing the effectiveness of the exogenous pancreatic enzymes. Non-acid-protected pancreatic enzymes may be necessary, or alternatively, the patient can open the capsule and consume the contents during a meal. All in all, attention must be paid to sufficient medication aimed at treatment success. The standard dose is 1 to 3 x 40 000 IU per day of lipase and the preparations should be taken at mealtimes. For snacks, generally 1 to 2 x 25 000 IU lipase are sufficient.

Weight loss after pancreatic carcinoma resection

Cachexia is common in patients with pancreatic carcinoma, and one of the strongest predictors of short survival (17). Preoperatively, more than half of patients lose over 5 kg body weight. Postoperatively, even after R0 resection, the patients continue to lose weight (14). The causes of weight loss include tumor progression, as well as pancreatic insufficiency (e.g. through pancreatic duct stenosis or pancreatic tissue deficiency caused through surgery). A small study showed that administration of pancreatic enzymes delayed weight loss even in patients with extensive and thus non-resectable pancreatic carcinoma (18).

Vitamin deficiency

If a partial gastric resection is also carried out, vitamin B_{12} deficiency arises due to a lack of "intrinsic factor," which has to be replaced by monthly intramuscular injections. B-vitamin deficiency is a particular issue in patients who continue to consume alcohol. Fat-soluble vitamin deficiency is somewhat unusual, but can be caused by continuing alcohol consumption, marked exocrine insufficiency, and/or severely limited fat intake (19). It can be detected via the measurement of serum 25-OH-vitamin D_3 (standard value: 30 to 60 ng/mL. Vitamin K deficiency can be assessed via the INR. The serum levels of vitamins A and E are unfortunately unreliable, but beta-carotine measurement can be useful.

The preparation previously used for intramuscular application to treat fat-soluble vitamin deficiency is no

longer available in Germany. It is, however, specially prepared in some pharmacies.

Diabetes mellitus

The incidence of diabetes increases with disease duration. Two large cohorts of around 200 and 500 patients with chronic pancreatitis were investigated in prospective long-term studies (20, 21). After around 10 years diabetes mellitus is present in 25% and after around 25 years in 80% of the patients. The frequency of diabetes was similar in surgically and non-surgically treated patients (20, 21), so that surgery alone can only rarely be made responsible for newly occurring diabetes. This is however not the case for left-sided resection, as very many islets are found in the pancreatic tail (20). Progression seems to be faster in the alcoholic forms of the disease than with non-alcoholic chronic pancreatitis (22). The form concerned is usually the pancreoprivic form of diabetes mellitus, which is classified as type IIIc. In addition, insulin deficiency counterregulation is also impaired (glucagon deficiency). As a result of this, the danger of hypoglycemia is especially high. The commonly applicable HbA1c limits should be set generously here (target HbA1c not below 6.5). Intensive patient education (dietary advice, specialist diabetes center follow up) is necessary. If compliance is good and the patient does not tend towards hypoglycemic episodes, intensified insulin therapy is possible. Treatment with oral antidiabetics is not useful under these conditions. Unfortunately, there are currently no evidence-based recommendations for this, so that this statement should be exclusively viewed as an expert opinion of the authors.

A particular problem exists in patients with chronic pancreatitis who continue to consume alcohol after surgery, which applies to approximately one quarter of patients (10). For them, food intake is irregular, alcohol consumption unpredictable, and the insulin dosage thus problematic. For these patient too, the primary aim is avoidance of hypoglycemic episodes, and even higher HbA1c values should be tolerated. Continuing alcohol and nicotine consumption shorten the life expectancy of these patients by around 10 years (23).

Pain

In approximately 80% of patients who underwent surgery for chronic pancreatitis, the postoperative analgesic requirement is lower, while the remaining 20% gain no benefit in terms of pain. Persistent pain can be related to progression of the underlying disease or result from complications (stomach ulcers, portal or splenic vein thrombosis, pseudocysts, mechanical cholestasis). Likewise acute on chronic attacks of pancreatitis with pain can occur. Investigation involves imaging procedures such as skilled ultrasound examination and computerized tomography as well as endoscopy of the upper gastrointestinal tract and corresponding laboratory tests. If no cause can be found for the pain, a chronic pain syndrome with chronic pancreatitis or with pancreatic carcinoma must be assumed and treated according to the WHO staging system (24).

Bile duct stenoses

Bile duct stenosis requiring treatment occurs in around 2% to 4% of patients. Interventional endoscopic treatment is often difficult after a classic Kausch-Whipple procedure, as the outlet of the bile duct cannot be reached. In this case either a percutaneous transhepatic or other surgical revision must take place.

Sequelae

Around 2% to 4% of patients with chronic pancreatitis suffer from pancreatic carcinoma; this corresponds to an increase in the relative risk by a factor of 20 to 40 (25). It should be stated that to date there is no reliable imaging procedure, which can aid in the detection of pancreatic carcinoma in a chronically inflamed gland. Chronic alcohol and nicotine abuse lead to cardiovascular diseases such as myocardial infarction and peripheral vascular disease as well as lung, esophageal, and head and neck malignancies. These tumors cause three to ten times more deaths than from pancreatic carcinoma (25) in this group, and they are therefore relevant for the overall prognosis of the patient. To avoid these sequelae the addiction problems must be discussed with the patient and appropriate help offered. While 70% of the patients are able to adjust their alcohol consumption (10), only very few manage to abstain from nicotine.

Conflict of interest statement
The authors declare no conflict of interest according to the guidelines of the International Committee of Medical Journal Editors.

Manuscript submitted on 3 March 2009, revised version accepted on 2 June 2009.

Translated from the original German by mt-g and Dr. Sandra Goldbeck-Wood.

REFERENCES

1. Adler G, Seufferlein T, Bischoff SC, et al.: S3-Guidelines „Exocrine pancreatic cancer“ 2007. Z Gastroenterol. 2007; 45: 487–523.
2. Oettle H, Post S, Neuhaus P, et al.: Chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial. JAMA 2007; 297: 267–77.
3. Traverso LW, Longmire WP: Preservation of the pylorus in pancreaticoduodenectomy. Ann Surg 1980; 192: 306–9.
4. Klinkenbijl JHG, VanDerSchelling GP, Hop WCJ, VanPel R, Bruining HA, HA, Jeekel J: The advantages of pylorus-preserving pancreaticoduodenectomy in malignant disease of the pancreas and periampullary region. Ann Surg 1992; 216: 142–5.
5. Diener MK, Knaebel HP, Heukaufer C, et al.: A systemetic review and meta-analysis for pylorus-preserving versus classical pancreaticoduodenectomy for surgical treatment of periampullary and pancreatic carcinoma. Ann Surg 2007; 245: 187–20.
6. Warshaw AL, Torchiana DL: Delayed gastric emptying after pylorus preserving pancreaticoduodenectomy. Surg Gynecol Obstet 1985; 160: 1–4.
7. Beger HG, Krautzberger W, Bittner R, Büchler M, Limmer J: Duodenum preserving resection of the head of the pancreas in patients with severe chronic pancreatitis. Surgery 1985; 97: 467–73.
8. Frey CF, Smith GJ: Description and rationale of a new operation for chronic pancreatitis. Pancreas 1987; 2: 701–7.

KEY MESSAGES

- Around 10 000 surgical pancreatic interventions are carried out per year in Germany.
- The sequelae can be caused either by the operation itself or otherwise by progression of the underlying disease. Among these are pain, weight loss, diarrhea, steatorrhea, and abdominal pain.
- These can be caused by both exocrine and endocrine insufficiency, low calorie intake, vitamin deficiency, or numerous complications such as pseudocysts, portal and splenic vein thrombosis, bile duct stenosis, etc.
- The recommendations on fat intake are less restrictive than in the past. A higher dietary fat content avoids (when tolerated or after adjustment of the enzyme dose) weight loss and a deficiency in fat-soluble vitamins.
- No follow up is recommended for patients without symptoms after pancreatic resection. Nevertheless regular clinical examination is probably sensible.

9. Müller MW, Friess H, Martin DJ, Hinz U, Dahmen R, Büchler MW: Long-term follow-up of a randomized clinical trial comparing Beger with pylorus-preserving Whipple procedure for chronic pancreatitis. Br J Surg 2008; 95: 350–6.
10. Strate T, Bachmann K, Busch P, et al.: Resection vs drainage in treatment of chronic pancreatitis: long-term results of a randomized trial. Gastroenterology 2008; 134: 1406–11.
11. Tanaka M, Chari S, Adsay V, et al.: International consensus guidelines for management of intraductal papillary mucinous neoplasma and mucinous cystic neoplasms of the pancreas. Pancreatology 2006; 6: 17–32.
12. Yekebas EF, Wolfram L, Cataldegirmen G, et al.: Postpancreatectomy hemorrhage: diagnosis and treatment: an analysis in 1669 consecutive pancreatic resections. Ann Surg 2007; 246: 269–80.
13. Welsch T, Büchler MW, Schmidt J: Surgery for pancreatic cancer. Z Gastroenterol 2008; 46: 1393–403.
14. Bachmann J, Heiligensetzer M, Krakowski-Roosen H, Büchler MW, Friess H, Martignoni ME: Cachexia worsens prognosis in patients with resectable pancreatic cancer. J Gastrointest Surg 2008; 12: 1193–201.
15. Maljaars PW, Peters HP, Mela DJ, Masclee AA: Ileal brake: a sensible food target for appetite control. A review. Physiol Behav 2008; 95: 271–81.
16. Siegmund E, Löhr JM, Schuff-Werner P: The diagnostic validity of noninvasive pancreatic function tests—a meta-analysis. Z Gastroenterol 2004; 42: 1117–28.
17. Maréchal R, Demols A, Gay F, et al.: Prognostic factors and prognostic index for chemonaïve and gemcitabine-refractory patients with advanced pancreatic cancer. Oncology 2007; 73: 41–51.
18. Bruno MJ, Haverkort EB, Tijssen GP, Tytgat GN, van Leeuwen DJ: Placebo controlled trial of enteric coated pancreatin microsphere treatment in patients with unresectable cancer of the pancreatic head region. Gut 1998; 42: 92–6.
19. Marotta F, Labadarios D, Frazer L, Girdwood A, Marks IN: Fat-soluble vitamin concentration in chronic alcohol-induced pancreatitis. Relationship with steatorrhea. Dig Dis Sci 1994; 39: 993–8.
20. Malka D, Hammel P, Sauvanet A, et al.: Risk factors for diabetes mellitus in chronic pancreatitis. Gastroenterology 2000; 119: 1324–32.
21. Ammann RW, Muellhaupt B: The natural history of pain in alcoholic chronic pancreatitis. Gastroenterology 1999; 116: 1132–40.
22. Keim V, Witt H, Bauer N, et al.: The course of genetically determined chronic pancreatitis. JOP 2003; 4: 146–54.
23. Lankisch PG: Natural course of chronic pancreatitis. Pancreatology 2001; 1: 3–14.
24. World Health Organization: Cancer pain relief. 3rd ed. Genf, 1996.
25. Pedrazzoli S, Pasquali C, Guzzinati S, Berselli M, Sperti C: Survival rates and cause of death in 174 patients with chronic pancreatitis. J Gastrointest Surg 2008; 12: 1930–7.

Corresponding author
Prof. Dr. med. Michael Poll
Heidkopfweg 11
32312 Lübbecke, Germany
poll.michael@web.de